Complexities of cardiomyopathy in septic shock

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Purpose of review
This review highlights the complex pathophysiology of myocardial dysfunction in septic shock and emphasizes the need for early and repeated hemodynamic assessments to improve outcome.

Recent findings
Septic cardiomyopathy is a complex, dynamic process driven by multiple mechanisms such as direct myocardial depression induced by host immune mediators (e.g., cytokines, nitric oxide) and/or bacterial toxins, and mitochondrial metabolic dysfunction. Recent echocardiography studies have described multiple unique hemodynamic clusters (phenotypes) that correlated with clinical outcomes. Similarly, serial echocardiography findings and mean arterial pressure abnormalities in patients with Streptococcal Toxic Shock Syndrome (StrepTSS) yielded three distinct hemodynamic groups that predicted mortality and morbidity. Because excessive use of fluids and/or vasopressors can be detrimental, especially in patients with microvascular injury or cardiomyopathy, application of the cardiovascular performance criteria of these different phenotypes could better inform management decisions in real time and improve outcome.

Summary
Septic cardiomyopathy is a dynamic, multidimensional response of the myocardium to infection involving both normal and dysregulated immune responses in which the measurable changes in myocardial function predict outcomes. This current paradigm mandates that functional parameters of cardiac performance be measured early and repeatedly throughout the disease course using echocardiography to guide treatment and improve outcome.

Keywords
cardiomyopathy, echocardiography, ejection fraction, mean arterial pressure, septic shock, streptococcal toxic shock syndrome

INTRODUCTION

Mortality from septic shock remains high and may be associated with profound myocardial dysfunction as well as vascular, metabolic and cellular abnormalities that contribute to multiple organ failure [1▪]. Early studies of sepsis assumed that systolic heart function was normal since cardiac output was high; therefore it was concluded that hypotension was solely the result of vasodilatation. Subsequent reports showed that some patients with septic shock had reduced left ventricular (LV) ejection fractions but, remarkably, normal cardiac outputs. LV dilatation was thus understood to be an important physiologic compensatory (adaptive) mechanism for maintaining output provided that patients received sufficient fluid administration to increase venous return (preload) and enhance ventricular performance. However, excessive fluid administration in patients with pulmonary edema may lead to increased mortality. Point-of-care ultrasonography has proven useful in predicting a patient's likely responsiveness to bolus fluid administration before such therapy is initiated. This technique can also be used to evaluate patients for complications of fluid accumulation (e.g., lung edema).

Increased after-load (vascular resistance) is another recognized mechanism of septic shock; here patients usually display peripheral cyanosis and cold extremities (cold shock) despite normal cardiac function. In this scenario, IV fluids alone may not correct blood pressure or restore tissue perfusion. Peripheral vascular dysfunction including coagulopathy and arterial vasoconstriction can result from microvascular injury mediated by immune complexes, increased shear forces or by microbial products such as exotoxins. Normal (or elevated)

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KEY POINTS

- Septic shock-associated cardiomyopathy is a complex, multidimensional response to, and consequence of, severe infection and is a critical determinant of outcome.
- Septic cardiomyopathy progresses in multiple, temporally distinct, stages that can be distinguished by analysis of clinical, laboratory and echocardiographic findings.
- Assessment of cardiac function early and throughout the disease course using echocardiography should be utilized to inform appropriate therapeutic interventions.
- Newer technologies applied to the complexities of septic cardiomyopathy hold promise for future precision medicine-based therapeutic approaches for this devastating condition.

peripheral vascular resistance in the face of reduced cardiac output is often associated with multiorgan dysfunction and increased mortality. Use of vasopressors may actually cause harm in such patients by further increasing peripheral vascular resistance such that vital organs and tissues are irreversibly damaged. Morbidity is also high in this setting; survivors may develop symmetrical gangrene of the digits or extremities that requires amputations or are left with permanent cognitive impairments. Thus, in many types of septic shock, excess fluid replacement and/or imprudent use of vasopressors may actually increase morbidity and mortality [2▪].

Noninvasive measurement of cardiac function by point-of-care echocardiography has demonstrated that some patients with septic shock exhibit reduced blood pressure and circulatory collapse due to impaired myocardial contractility [3,4▪]. Such findings have prompted a paradigm shift such that it is now deemed prudent to dynamically measure central venous pressure, monitor arterial pressure, evaluate renal function, measure cardiac performance by echocardiography and then utilize these evolving data to direct decisions about fluid replacement, vasopressors, colloid, and renal dialysis. In patients that progress to late stages of cardiomyopathy, venoarterial extracorporeal membrane oxygenation (VA-ECMO) or even cardiac bypass may be necessary.

Thus we are beginning to appreciate that septic shock has many different, highly dynamic, and overlapping physiologic patterns, some of which predict worse outcomes while others represent potentially beneficial adaptive responses to serious infection [4▪,5▪]. Such complexity significantly reduces the value of a "one size fits all" approach to treatment. Instead such improved understanding suggests that hemodynamic management must be individually adapted during the course of septic shock. This is especially true when pathogens such group A streptococcus have multiple mechanisms to cause shock and organ failure including toxin-mediated vascular and myocardial dysfunction (see below).

However, tools to distinguish between these responses in real time have only recently been investigated. In the last few years, studies combining echocardiography with clinical data have defined 3–5 unique cardiovascular clusters (phenotypes) that reflect different underlying molecular mechanisms and relate to clinical outcomes [6,7,8▪]. Similarly, machine learning (ML) technology has been recently applied to septic cardiomyopathy. A 2021 prospective clinical study utilized an exploratory ML approach in which echocardiographic data, clinical findings, next generation genomic parameters, and circulating biomarker levels were used to characterize the extent of, or risk for, myocardial injury and cardiac dysfunction in patients with septic shock [9]. It also proved useful in determining the underlying mechanisms of septic cardiomyopathy at molecular level and in identifying a role of complement, coagulation, and inflammation pathways in the pathophysiology of myocardial injury.

MECHANISMS OF CARDIOVASCULAR DYSFUNCTION IN SEPTIC SHOCK

The pathophysiologic mechanisms of the various forms of septic cardiomyopathy have been intensively studied but not fully defined. Circulating endogenous shock-promoting cytokines such as macrophage-derived tumor necrosis factor alpha (TNFα) and interleukin (IL)-1β have long been understood to be key players. In gram negative sepsis, endotoxin is considered the primary inducer of these mediators. Similarly, surface components of various gram positive pathogens (e.g., peptidoglycan) can also induce their production. However, unlike gram negative organisms, some gram positive pathogens such as *Staphylococcus aureus* and group A streptococcus (GAS) produce superantigens that also elicit cytokine production from lymphocytes (e.g., TNFβ, IFNγ, IL-2).

More recently, studies have implicated other highly complex mechanisms contributing to myocardial damage in septic shock, including reduced myocardial circulation, direct myocardial depression, and mitochondrial dysfunction [4▪], the latter leading to changes in myocardial oxidative phosphorylation, local production of cell-damaging reactive oxygen radicals, reprogramming of cardiomyocyte energy metabolism, and apoptosis [4▪].

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CARDIOVASCULAR DYSFUNCTION IN GROUP A STREPTOCOCCAL TOXIC SHOCK SYNDROME

In our initial series [10], 50% of patients with streptococcal toxic shock syndrome (StrepTSS) responded to intravenous fluid administration, suggesting that inadequate preload and peripheral dilatation of vascular beds were important clinical features. In that study, 1 of 20 patients also developed dilated cardiomyopathy [10]. Since then one small series [11] and a case from the Massachusetts General Hospital [12] have also reported cardiomyopathy in StrepTSS.

GAS can cause cardiovascular dysfunction by several novel mechanisms. These include the ability of streptolysin O (SLO) to directly reduce myocardial contractility via disruption of normal calcium handling mechanisms [13]. In addition, SLO can induce formation of occlusive intravascular platelet/neutrophil aggregates that cause ischemic necrosis of tissue [14]. Further, our experimental studies have shown that GAS can induce cardiomyocyte-derived cytokines, including IL-1β, TNF-α, IL-6 and MIP-2 [15]. Even small amounts of cardiomyocyte-derived TNF-α produced in the microenvironment of the heart may contribute to the cardiac contractile dysfunction observed in patients with StrepTSS-associated cardiomyopathy.

These varied mechanisms may in part explain the difficulty in treating StrepTSS. Despite advances in critical care management of septic shock, mortality among patients with StrepTSS has remained between 30–60% over the last three decades [10,16–18] and survivors often have life-changing disability including amputation, blindness and cognitive impairment. Host factors, such as age > 60 and underlying diseases have been associated with the highest mortality, yet the specific hemodynamic factors which contribute to mortality and complicate contemporary management have not been fully elucidated. To further highlight this issue, we present serial hemodynamic findings and outcomes of twenty (20) patients (Table 1, Supplemental Digital Content, http://links.lww.com/COID/A55) who met the clinical definition of StrepTSS and had undergone invasive monitoring or received echocardiograms or both.

Patient demographics

Fifteen of the 20 (75%) StrepTSS cases were female. The patients ranged in age from 5.5 to 53 years (mean: 32.6 years; median: 35 years) and all were previously healthy with no underlying conditions. The portals of entry were: vaginal mucosa (4), respiratory tract (5), skin (4), and unknown (7). Types of infection included: necrotizing fasciitis/myonecrosis (7), pneumonia/empyema (4), uterine infection (3), peritonitis (3), joint space infection (2), and pharyngitis (1). Eleven patients (55%) had necrotizing infection of muscle, chest wall or uterus and 14/20 (70%) had GAS bacteremia. Three patients developed postpartum StrepTSS but all had had uncomplicated pregnancies and delivered healthy babies.

Cardiovascular dynamics

Seventy-five percent of patients had been seen by physicians in private offices or in emergency departments 12–24 h prior to admission and all had normal blood pressures but modest tachycardia (mean: 100 beats/min). During the first 24 h period following admission (defined here as Stage I), the average mean arterial pressure (MAP) was 47.25 mmHg (SD 8.4, Table 1) and all had marked tachycardia (mean: 134 beats/min). All patients were resuscitated with fluid boluses of normal saline (1–2 L) in the emergency department or on admission to the intensive care unit. The exceptions were patients #5 and #10 who were 10 and 5.5 years of age, respectively; these patients received 15–30 cc/kg boluses. Among adults, ~5 L of normal saline was given in the first 6 hrs and all received 10–20 L of intravenous fluid over the first 24 h period. Diffuse capillary leak and rapidly declining serum albumin were evident.

Invasive monitoring provided serial hemodynamic measurements in 14/20 patients. Fluid resuscitation increased MAP and central venous pressure (CVP) to 64.95 mmHg and 10 – 12 mmHg, respectively (Stage II; Table 1). At this time, cardiac index (CI) was 5.9 l/min/m^2 (Fig. 1); however by 48 hrs (Stage III), CI dropped to $\leq$ 2.78 L/min/m^2 (Fig. 1) prompting both increased fluid administration to maintain CVP at 8–12 mm Hg and the use of a variety of pressor agents (Table 1). Despite these efforts, CI continued to decline and by 72 h, reached a nadir of 2.16 L/min/m^2 (SD 0.84) and remained low at 96–120 h (2.39 and 2.28 L/min/m^2, respectively) (Fig. 1). In surviving patients who had CI measurements taken at 10 days post admission (Stage IV), the CI rose to >5 L/min/m^2 (Fig. 1).

Echocardiographic studies, performed in 15/20 patients, demonstrated declining ejection fractions (25%; range 18–35%) and progressive global hypokinesia in 14/15 patients. One patient had segmental akinesia of the lateral wall, septal wall and apex. In three survivors, echocardiograms done 180–660 days post StrepTSS demonstrated normalization of reduced ejection fractions (>50%) and resolution of global hypokinesia.

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Table 1. The relationship between MAP and outcomes in patients with acute cardiomyopathy associated with streptococcal toxic shock syndrome

			Stage III			
	Stage I ***N*** **= 20**	**Stage II** ***N*** **= 20**	**Group 1: MAP < 50** ***N*** **= 6**	**Group 2: MAP 50 -65** ***N*** **= 7**	**Group 3: MAP > 65** ***N*** **= 7**	**Stage IV** ***N*** **= 9**
MAP[a] (mmHg ± standard deviation)	47.25 ± 8.4	64.95 ± 17.0	41.17 ± 3.4	58.14 ± 5.1	85.57 ± 19.4	72.78 ± 7.0
CI[b] (l/min/m^2 ± standard deviation)	ND[c]	5.9 ± 1.15	1.9 ± 0.25	1.72 ± 0.45	2.78 ± 0.64	5.2 ± 1.48
Mortality (%)	0	0	100	28.5	43	0
Major morbidity (%)	0	0	NA[d]	0	100	44
■ Symmetrical gangrene				0	100	44
■ Four limb amputation				0	57	44
■ Encephalopathy				0	14.2	11
■ Blindness				0	14.2	11
Limited morbidity (%)	0	0	0	28.5	100	55
■ Symmetrical gangrene of distal digits				28.5	100	55
Vasopressor usage (%)						
■ None			0	29	0	
■ Dopamine			83	57	86	
■ Epinephrine			67	29	71	
■ Neosynephrine (phenylephrine)			33	14	29	
■ Levophed (norepinephrine)			33	43	57	
■ Dobutamine			17	43	14	
■ Two or more of the above agents			50	57	100	

CI, cardiac index; MAP, mean arterial pressure.
[a]Mean arterial pressure.
[b]Cardiac index.
[c]Not Done.
[d]Not applicable.

The relationship of cardiac parameters to clinical outcomes

During Stage III, three distinct patterns of hemodynamic responses were apparent (Table 1).

(1) Group 1 ($N = 6$) had low CI and low MAP (means: 1.9 L/min/m^2 and 41.17 mmHg, respectively);
(2) Group 2 ($N = 7$) had low CI and moderate MAP (means: 1.7 L/min/m^2 and 58.14 mmHg, respectively) and
(3) Group 3 ($N = 7$) had moderate CI and high MAP (means: 2.78 L/min/m^2 and 85.57 mmHg, respectively).

The mortality rate and the incidence of severe morbidity varied greatly between these hemodynamic groups (Table 1). For instance, the mortality of patients in Group 1 (low CI/low MAP) was 100%; this mortality rate was statistically associated with a sustained MAP of <50 mmHg ($P < .05$). In contrast, the mortality in Group 2 (low CI/moderate MAP) was 28.5% and survivors had limited morbidity consisting of gangrene of one or more digits. Group 3 (moderate CI/high MAP) had higher mortality than Group 2 (i.e., 43% vs. 28.5%, respectively) despite a higher CI (2.78 L/min/m^2) and also had severe morbidity: 100% had symmetrical gangrene of digits, 85.5% had amputation of at least 1 extremity, 57% had amputation of 4 extremities, 14.2% had severe permanent encephalopathy, and 14.2% had total blindness (Table 1). Development of severe morbidity was strongly associated with a MAP >65 mmHg ($P = 0.007$). Vasopressor usage among patients in Group 3 was more intense than the other two groups; 100% of patients in Group 3 received 2 or more agents, the most frequently used being dopamine, epinephrine and norepinephrine (Table 1). It should be noted that in Group 3, the average MAP was very high (85.57 mmHg), a value much higher than that recommended (60–65 mmHg) for septic patients receiving pressor agents [19].

A graph relating the CI, MAP, serum lactate and serum bicarbonate in a representative patient from Group 3 is depicted in Fig. 2. Note that the CI dropped from 6 to ≤3 L/min/m^2 while the MAP rose to >85 mm Hg in response to norepinephrine (10 μg/kg/min) plus dopamine (8 μg/kg/min). This increase in MAP was associated with rising lactic acid concentrations from 2 to >20 mmoles/L and a

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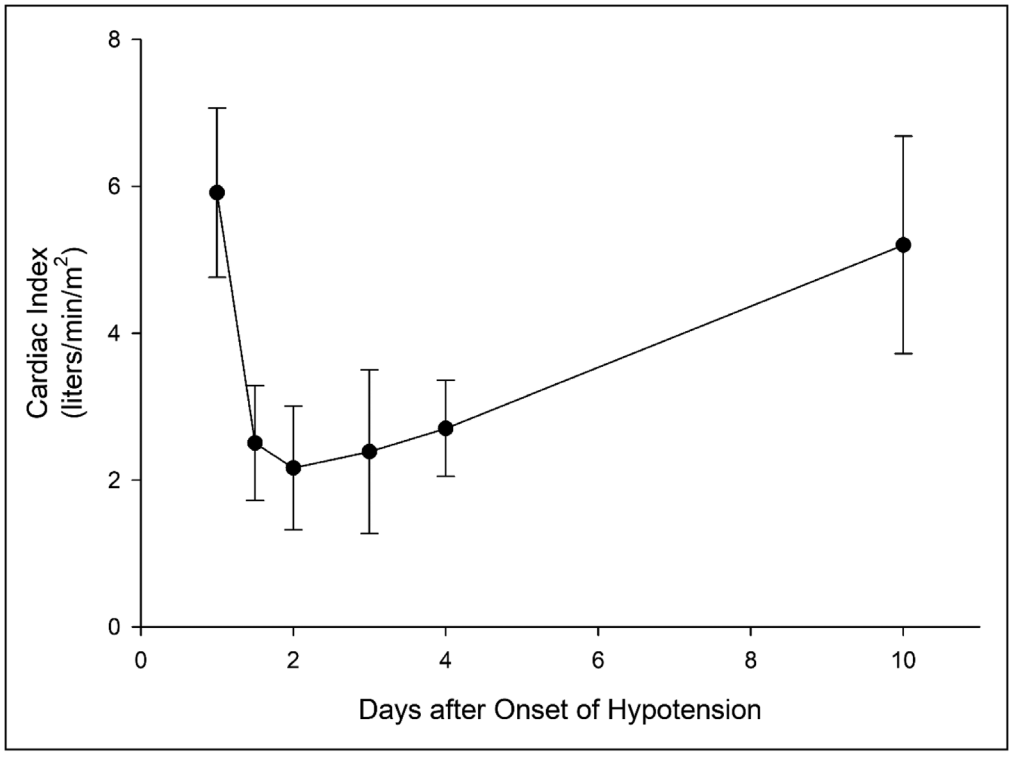

FIGURE 1. Dynamics of cardiac index in patients with StrepTSS. Fourteen of the 20 patients who met the criteria for StrepTSS underwent invasive monitoring of cardiac function. Data shown are the means of cardiac index ± standard deviation over the disease course in these patients.

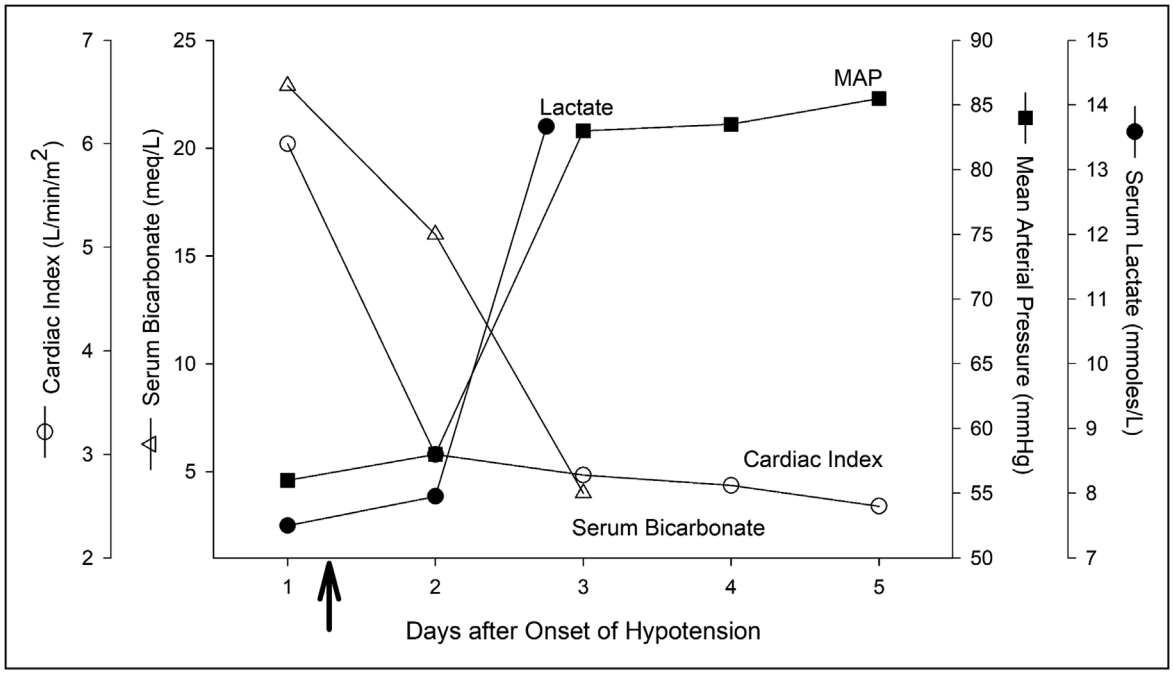

FIGURE 2. Relationship of CI, MAP, serum lactate and serum bicarbonate in a representative StrepTSS patient from Group 3 (moderate CI, high MAP). Arrow indicates time of administration of norepinephrine (10 μg/kg/min) plus dopamine (8 μg/kg/min). Note that the pressor-induced rise in MAP was associated with a profound drop in CI, rising lactic acid concentration and a simultaneous drop in serum bicarbonate. During this time, an echocardiogram revealed a severely reduced ejection fraction (20%) and global hypokinesia. This patient developed profound symmetrical gangrene of all four extremities and died on the 5th hospital day. CI, cardiac index; MAP, mean arterial pressure.

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simultaneous drop in serum bicarbonate from 14.3 to 8.0 meq/L. During this time, an echocardiogram revealed an ejection fraction of 20% and global hypokinesia. This patient developed profound symmetrical gangrene of all four extremities and died on the 5th hospital day.

Coagulopathy

Laboratory evidence of coagulopathy [i.e., increased prothrombin time (PT) and partial thromboplastin time (PTT), thrombocytopenia, and increased fibrin degradation products (FDP)] was present in 9 patients (data not shown), yet the serum fibrinogen level was normal or elevated in all patients. Two patients had clinical evidence of DIC such as petechiae and ecchymosis and both of these developed symmetrical gangrene. Six additional patients developed symmetrical gangrene but did not have clinical or laboratory evidence of DIC yet all had received vasopressors.

Histopathology of cardiac tissue

Gross examination of postmortem cardiac tissue demonstrated no evidence of myocardial infarction. The ventricular chambers were not visibly dilated, the valve leaflets were intact and devoid of fibrin clot and no vegetations were found. Coronary arteries were patent without evidence of significant arteriosclerosis, thrombosis or embolization. Rare microvascular thrombi were observed despite the patency of large coronary arteries described above. The myocardium was devoid of acute or chronic inflammatory cells though modest edema was noted.

Statistical analyses

For comparative analysis, MAP values in clinical stage III were categorized into three ranges, <50, 50–65 and >65 mmHg, respectively. The MAP raw data was transformed into categorical variables (yes or no) based on whether they fell into one of these three ranges. Mortality and the presence of significant morbidity (i.e., gangrene, amputation, encephalopathy, blindness) were also transformed into categorical variables. Association between the MAP and outcome (alive vs. deceased) or the development of severe complications (presence vs. absence) was assessed by Fisher's exact test with the level of significance set at $P \leq 0.05$.

DISCUSSION

Septic cardiomyopathy is now recognized as a dynamic, multidimensional response of the myocardium to infection involving both normal and dysregulated immune responses in which the measurable changes in myocardial function predict outcomes. Thus, cardiac function must be carefully and dynamically monitored in patients with all forms of septic shock to reduce mortality and morbidity.

The study described above provides an example of the dramatic differences in cardiac function in different stages of StrepTSS. Overall 55% of patients died – a mortality rate that is consistent with other reports of StrepTSS [10,16–18,20,21]. Serial measurements demonstrated that myocardial dysfunction evolved in distinct stages. Stage I occurred 3–6 days after the onset of symptoms of infection and was characterized by hypotension and marked tachycardia. Fluid resuscitation improved MAP and maintained a high CI (Stage II). Thus, Stages I-II are likely similar to the state of high cardiac output and low systemic vascular resistance described for gram negative sepsis [22,23]; such patients generally have low preload and respond to fluid administration with increased CVP and a resultant increase in stroke volume that is, in part, related to increased diastolic pressure and subtle stretching of myocardial fibrils. Modest dilation of the left ventricular chamber increases the strength of contraction (dp/dt), stroke volume and cardiac index [22,23]. In the current study, increased CI in Stage II suggests that myocardial contractility was normal early in StrepTSS.

Stage III of StrepTSS-associated cardiomyopathy began ~48 h after Stage I and was characterized by low CI despite adequate preload, tachycardia and low SVR. Reduced ejection fractions, dilated left ventricle and marked hypokinesia were documented in 15 patients by echocardiography. This phase of StrepTSS-associated cardiomyopathy is strikingly different than that described in patients with gram negative sepsis [23,24]. Specifically, both survivors and nonsurvivors of gram negative shock had an elevated CI early (12–24 h) that either remained elevated or gradually returned to normal over 4 days [24]. It was concluded that for gram negative sepsis, "a low cardiac index is, in fact, uncommon even in very late stages of septic shock" [23,24].

StrepTSS patients in Group 3 had excessively increased MAP (85.57 mmHg) but persistently low CI (mean 2.78 L/min/m^2) in response to pressor agents. Mortality was 43% and all survivors had major morbidity including permanent brain damage and symmetrical gangrene necessitating multiple amputations. Notably, very high MAP in response to norepinephrine and dopamine in one patient resulted in declining CI and dramatic worsening of metabolic acidosis. The consequence of such a decline in perfusion and low CI is nicely stated by Beale *et al.*, "Higher values [of MAP] should be avoided during norepinephrine therapy because

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elevated cardiac afterload may be deleterious, especially in cases of severe underlying cardiac dysfunction" [25].

As mentioned previously, the pathophysiology of myocardial dysfunction in StrepTSS is particularly complex. Somatic components and soluble exotoxins of group A streptococcus are potent inducers of circulating leukocyte-derived cytokines, lymphokines and myocardial depressant factors. Moreover, these bacterial factors can elicit cardiomyocyte-derived mediators within the microenvironment of the heart itself. Further, streptolysin O can cause direct loss of myocardial contractility via its ability to inhibit normal calcium handling mechanisms. Lastly, streptococcal exotoxins can also cause direct microvascular injury, leading to capillary leak and/or thrombosis in the peripheral vasculature, leading to tissue perfusion deficits and concomitant reductions in venous return to the heart.

Given this complexity, cardiomyopathy associated with StrepTSS poses unique challenges to critical care management. Fluid resuscitation strategies, which have been well defined for septic patients in general, are confounded by five features characteristic of StrepTSS: diffuse capillary leak; profound hypoalbuminemia that may require replacement with colloid rather than crystalloid [26]; bacterial toxin-mediated hemolysis that may require aggressive transfusions of packed red blood cells; renal failure that precedes hypotension and may require dialysis; and characteristically low serum calcium levels (both ionized and nonionized). Emergent surgery for source control is vital but may be difficult in those patients who are critically ill due to cardiomyopathy and profound hypotension. Since many of these factors may contribute to hypovolemia, dynamic measurements are crucial to evaluate fluid resuscitation efforts.

Our data suggest that StrepTSS patients with persistently low MAP and low CI should have echocardiograms to assess myocardial function. Following adequate fluid resuscitation, such patients may benefit from vasopressors however critical care guidelines provide both general recommendations and a few cautionary notes [27]. Dopamine in doses of $<5\,\mu g/kg/min$ enhances renal perfusion, yet at higher doses (5–10 $\mu g/kg/min$), beta-1-adrenergic effects predominate, resulting in increased cardiac contractility and heart rate. Enhancement of cardiac output by 34% has been observed among septic patients with refractory hypotension, largely due to increased stroke volume but with little effect on SVR [28]. Thus, dopamine's utility may be greatest in patients with decreased myocardial function who remain hypotensive, a situation described in some patients in the present series.

Dobutamine stimulates beta-1 and beta-2 adrenergic receptors and increases CI by increasing stroke volume and heart rate. If used in the presence of low MAP it should be combined with a vasopressor such as norepinephrine [25]. In one report dobutamine increased CI in patients with staphylococcal toxic shock syndrome [29]. Epinephrine increases MAP by increasing CI and stroke volume but also increases SVR, reduces regional blood flow, increases serum lactate and reduces blood pH. Norepinephrine generally increases MAP by increasing SVR with little change in heart rate or CI and may reduce renal perfusion. Phenylephrine, a selective alpha-1 adrenergic receptor agonist, increases CI in patients with low to normal CI ($3.3\,L/min/m^2$) but also increases MAP by increasing SVR.

While the vasopressors discussed above may be useful in some septic shock settings, they may worsen CI by increasing afterload in StrepTSS patients with acute cardiomyopathy. Further, intense pressor-induced vasoconstriction in the face of low CI may directly reduce tissue perfusion and contribute to symmetrical gangrene in StrepTSS. Vasopressors may also contribute indirectly to ischemic necrosis of tissue by exacerbating GAS toxin-induced vascular occlusion [14] by increasing microvascular sheer forces [30,31]. Thus, to maximize the efficacy of these agents and reduce complications, their use in patients with StrepTSS should be based on information gained from early and successive monitoring of cardiac function.

In the StrepTSS patients described here, some patients underwent cardiac bypass with assist devices. In a recent retrospective study, 82 septic patients with cardiomyopathy were evaluated and treated with venoarterial extracorporeal membrane oxygenation (VA-ECMO). Patients had a mean CI of $1.5\,L/m^2$ and mean left ventricular ejection fraction (LVEF) of 17%. Compared to 130 comparable controls, survival was 60% in the treatment group compared to 25% in the control group [32▪]. This is truly remarkable and points out the importance of practitioners being very quick and aggressive in monitoring cardiac function in sepsis.

CONCLUSION

Management of septic shock has benefited from a more in-depth understanding of the cardiovascular responses to severe infection. Such knowledge has compelled dynamic measurements of central venous pressures, peripheral blood pressures, renal function, oxygen saturations, cardiac silhouettes and cardiac outputs using both basic and advanced monitoring and imaging techniques. In StrepTSS where cardiomyopathy, peripheral vasoconstriction

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and/or intravascular occlusion can each contribute to mortality and life-altering morbidity, incorporation of these techniques early and throughout the disease course is vital to direct the appropriate use of fluids and vasoconstrictors to maximize their efficacy and minimize severe complications. Improved survival with newer treatments such as VA-ECMO are encouraging for patients with septic cardiomyopathy and further underscore the importance of appropriate cardiovascular evaluations early and throughout the course of septic shock. Lastly, powerful emerging technologies such as machine learning may facilitate sepsis phenotype identification and usher in a new era of precision medicine-based therapies for septic cardiomyopathy.

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Conflicts of interest

There are no conflicts of interest.

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A very encouraging clinical study demonstrating a dramatic improvement in survival among patients with cardiogenic septic shock who received extracorporal membrane oxygenation (ECMO) support.

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